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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/522,826	07/21/2005	Viktor Menart	LB/G-32991A/LEK	4902

1095 7590 09/27/2007

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
MACFARLANE, STACEY NEE	

ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
09/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,826	MENART ET AL.	
	Examiner	Art Unit	
	Stacey MacFarlane	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12-17,19-27 and 29-31* is/are pending in the application.

4a) Of the above claim(s) *2,27 and 29-31* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 3-10, 12-17 and 19-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/31/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I, Claims 1, 3-10, 12-17 and 19-26 and the species G-CSF, in the reply filed on August 24, 2007 is acknowledged.

2. Claims 2, 27 and 29-31 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on August 24, 2007.

3. Claims 1, 3-10, 12-17 and 19-26 in so far as they read upon the elected species, will be considered upon their merits.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 1, 3-10, 12-17 and 19-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

6. Claims 1 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: For Claim 1 the active steps by which the process is performed. For example, the active steps and elements of the parameters or conditions and the adjustments made so that the amount of protein is

increased in inclusion bodies. For Claim 9, the means by which parameters are adjusted in order to achieve the process. Furthermore, where a claim sets forth a plurality of elements or steps, each element or step of the claim should be separated by a line indentation. There may be plural indentations to further segregate subcombinations or related steps. See 37 CFR 1.75 and MPEP 608.01(i)-(p).

7. The term "increased" in claim 1 is a relative term which renders the claim indefinite. The term "increased" is not defined within the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

8. Claims 19 and 20 are vague and indefinite in so far as they employs the terms "GYST", "GYSP", "LYSP", "LYST", "LBON" and "GYSPON" as limitations. The terms appear to be novel and all abbreviated terms must be spelled out upon their first appearance within the claims.

9. Claim 12 recites the limitation "the inducer" in claim 9. There is insufficient antecedent basis for this limitation in the parent claim.

10. Claim 21 recites the limitation "the additive" in claim 9. There is insufficient antecedent basis for this limitation in the parent claim.

11. Claims 4-10, 13-17 and 22-26 are indefinite for depending from indefinite claims.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Weickert et al. Applied and Environmental Microbiology, 63(11): 4313-4320, published November 1997.

14. Claim 1 is broadly drawn to a process for the production of a protein comprising the expression of said protein as a heterologous protein, wherein at least one of the parameters or conditions, is adjusted in such a way that the amount or proportion of the heterologous protein after expression is increased in said inclusion bodies.

15. The Weickert reference teaches a process for production of a heterologous protein (hemoglobin) wherein several parameters (i.e. temperature and concentration of inducer) are regulated and the resulting proportion of correctly folded protein in inclusion bodies is assessed (See Figures 1 and 2). The Weickert reference teaches the broadest embodiment of the instant claims.

Claim Rejections - 35 USC § 102/103

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

18. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

19. Claims 1, 3-10, 12-17, and 19-26 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Jeong et al. Protein Expression and Purification 23: 311-318, published November 2001.

20. Claims 1, 3-10, 12-17, and 19-26 are drawn to a process for the production of a protein comprising the expression of said heterologous G-CSF (Claim 4) in *E. Coli* (Claim 6), wherein at least one of the parameters or conditions of Claim 9, is adjusted in such a way that at least 10% of the heterologous protein relative to total protein is produced in inclusion bodies that can be dissolved under non-denaturing conditions. Dependent claims recite cultivation between 20-30°C, induction with IPTG and further comprising washing the inclusion bodies.

21. The Jeong et al. reference teaches methods for the production of a correctly folded recombinant human granulocyte-colony stimulating factor (hG-CSF) protein in the inclusion bodies of *E. Coli*. The prior art reference teaches that as high as 48% of total protein produced was hG-CSF (Page 314, line bridging columns). Thus, teaching

the "at least 10%" requirement of Claim 7. Furthermore, the Jeong reference teaches soluble protein was extracted by sonication under non-denaturing conditions (page 313, lines 13-18). The process as taught by Jeong et al. teaches fed-batch cultivation at 30°C (*Id*, line 4) and the induction with IPTG of 1mM, thus teaching "about 0.4mM" IPTG of Claim 15 as well as the requirements of claims 9-10, and 12-14, 16-17, 22 and 23-26. Additionally the reference teaches the process to further comprising several washing steps in phosphate buffer, acetic acid buffer and/or Tris/HCl buffer at concentrations in the range of 1mM to 10mM (page 313, section on *Purification of hG-CSF Protein*), teaching the limitation of claims 23 and 24. The reference further teaches the recombinantly produced hG-CSF that is correctly folded (Figure 6), teaching the requirement of Claim 1. Lastly, the cultivation media of the reference is disclosed as tryptone with yeast extract and sodium chloride, absent evidence to the contrary this media anticipates the media requirements of Claims 19-20. Furthermore, any discrepancies between the media or reagents of the claims and those of the reference are deemed to be *prima facie* obvious based on optimization of a known process, or at least an obvious variant by substitution of a known prior art element (See *KSR*, at 1742, 82 USPQ2d at 1390, citing *Dystar* 464 F.3d at 1368, 80 USPQ2d at 1651).

Double Patenting

22. Applicant is advised that should claim 3 be found allowable, claim 4 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof, in view of Applicant's election of G-CSF species in the Response to Election/Restriction filed July

24, 2007. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Conclusion

16. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacey MacFarlane whose telephone number is (571) 270-3057. The examiner can normally be reached on M,W and ALT. F 6 am to 3 pm, T & R 5:30 am - 4 pm..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a

USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Stacey MacFarlane
Examiner
Art Unit 1649

SNM

OLGA N. CHERNYSHEV, PH.D.
PRIMARY EXAMINER